REMARKS

I. STATUS OF THE CLAIMS.

Claims 184-190, 201, 204 and 207-216 were examined. Claims 184-190, 201, 204-207, and 210-212 are presently pending. Claims 208-209 and 213-216 are canceled herein without prejudice to subsequent renewal, including in a continuation or divisional application, which cancellations are not made for reasons relating to patentability. Claims 184, 186-190, 201, 204, 210, and 211 have been amended as discussed in greater detail below. All of the amendments herein are fully supported by the specification and none of the amendments constitutes new matter.

Applicants thank Examiners Carolyn L. Smith and Marjorie Moran for their time and courtesy during the telephone interview held on September 22, 2005, during which the pending claims and Office Action dated April 28, 2005 were discussed, including the rejection under 35 U.S.C. § 112, first paragraph regarding alleged lack of scope of enablement of claims 208, 209, and 213-216 and the rejection under 35 USC § 112, second paragraph regarding the alleged method steps in claims 208 and 209. Applicants thank the Examiners for their clarification and helpful suggestions.

II. DOUBLING PATENTING.

The Examiner states that "should claims 184, 188, 201, 204, 208-211, and 213-216 be found allowable, claims 184, 188, 201, 204, 208-211, and 213-216 will be objected to under 37 CFR § 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim." Office Action, page 2. The Examiner takes the position that claim 208 "appears to be reciting a property of the isolated or recombinant polypeptide of instant claim 184" and that "properties are inherent to a product and do not further limit the structure of the product." *Id.* Applying similar reasoning, the Examiner also concludes that claim 209 is a duplicate of claim 188, claim 213 is a duplicate of claim 201, claim 214 is a duplicate of claim 204, and claim 215 is a duplicate of claim 210.

Applicants note that the Examiner has characterized her findings as both: (1) a double patenting rejection; and (2) an objection based upon allegedly duplicate claims. This objection and/or rejection is respectfully traversed as follows.

Double patenting precludes an Applicant from obtaining more than one valid patent for either the same invention or an obvious modification of the same invention. Notably, the Examiner does not point to any other patent or application by Applicants that claims the same invention or an obvious modification of the same invention as claimed in the instant application. The Examiner provides no basis for a double patenting rejection. This rejection is improper and should be withdrawn.

Furthermore, none of the claims is a duplicate of any other claim. No rejected claim has the same wording as any other claim. Nor is the content of any rejected claim so close to that of another claim that it covers exactly the same thing as another claim. Applicants are allowed to determine the number and scope of their claims, and Applicants have a right to claim their invention in a reasonable number of ways. Indeed, courts have held that a mere difference in scope between claims is sufficient. Applicants respectfully submit that this duplication objection is improper and should be withdrawn.

Nevertheless, while not conceding to the validity or correctness of this rejection or objection (however framed), it has nevertheless been mooted by cancellation of claims 208-209 and 213-216 without prejudice to subsequent renewal.

III. REJECTIONS UNDER 35 USC § 112, FIRST PARAGRAPH.

Claims 208, 209, and 213-216 were rejected under 35 USC § 112, first paragraph, "because the specification, while being enabling for 4-fold increases in T cell proliferation using a certain combination of polypeptides, does not reasonably provide enablement for a 4-fold increase under any conditions as currently encompassed by the broadly stated limitations of the polypeptides of claims 184 and 188 in the presence of any p35 subunit of human interleukin-12 compared to any other combination of p40 and p35 subunits human interleukin-12." Office Action, page 5. The Examiner contends that the specification does not enable any person skilled

in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims. *Id.* The Examiner state that:

> The specification (page 16, first paragraph) states that SEQ ID NO:1 is a modified p40 nucleic acid sequence that encodes SEQ ID NO:8. The specification on page 30, starting on last paragraph, teaches testing for T-cell proliferation activities in culture supernatants of cells co-expressing various exemplified p40 nucleic acids plus wild-type p35 nucleic acid in comparison to supernatants of control cells co-expressing wild type p40 plus wild type p35 nucleic acids, as shown in Figures 2-6. The specification states that the data show that cells co-expressing a modified p40 nucleic acid with a wild type p35 nucleic acid secrete biologically active protein with 4-fold as much to as much as 64-fold higher T-cell proliferative activity than cells expressing wild type p40 plus wild type p35 nucleic acids. Table 1 shows C-22 (SEQ ID NO:1 which encodes SEQ ID NO:8) with a ~32 to 64 fold increase compared to control. On page 33 (first full paragraph) of the specification, it is stated that relative amounts of modified heterodimeric protein and wild-type heterodimeric protein were quantitated with modified nucleic acids tending to promote enhanced production of modified heterodimers as compared to wild-type heterodimers. The specification states on page 34, line 11, that purified C2-22 (SEQ ID NO:1)/wild type p35 heterodimer exhibited about a 4-fold higher proliferative activity than the compared control of wild type p40/wild type p35, as seen in Figure 9. Claims 208 and 209 state that there is a 4-fold increase in T cell proliferation with the polypeptide of instant claims 184 and 188, respectively, in the presence of a p35 polypeptide subunit of human interleukin-12 compared to the proliferation of T cells of a [sic] p40 and p35 polypeptide subunits [sic] of human interleukin-12. *It is noted that SEQ ID NO:8 could represent the latter mentioned p40 polypeptide subunit above, such that the comparison could essentially be a duplication resulting in no 4-fold increase.*"

Id. at pages 5-6 (emphasis added).

Additionally, the Examiner finds that "a comparison of (A) C2-22 (SEQ ID NO:1)/R2-42 (SEQ ID NO:16, modified p35 subunit) heterodimer as well as (B) C2-22 (SEQ ID NO:1)/R2-157 (SEQ ID NO:24, modified p35 subunit) heterodimer both show ~ 8-fold increase compared to wild types p40 and p35 subunit heterodimers, such that a comparison of (A) and (B) would not produce a 4-fold increase." *Id.* at page 6. The Examiner is of the view that while there is written support for 4-fold increases, "there are no experimental examples that

specifically state an exact 4-fold increase as recited in these claims" and "[f]urther experimentation would be required to determine which combinations resulted in exact 4-fold increases over other heterodimers." Based on these findings, the Examiner concludes that "claims 208 and 209 do not appear fully enabled for every modified and wild type heterodimer combinations providing 4-fold increases." *Id.* This rejection is respectfully traversed as follows.

First, Applicants respectfully submit that the Examiner has misread claims 208 and 209. Claim 209, which is dependent upon claim 188, specifies an isolated or recombinant polypeptide which comprises a sequence that is at least 95% identical to the full length of the sequence of SEQ ID NO:8 and induces a 4-fold increase in the proliferation of T cells in the presence of a p35 polypeptide subunit of human IL-12 compared to the proliferation of T cells induced by a p40 polypeptide subunit of human IL-12 in the presence of the p35 polypeptide subunit of human IL-12. The claimed polypeptide is not a wild-type p40 polypeptide subunit of human IL-12, as suggested by the Examiner. See, e.g., Office Action, page 6, lines 7-9. For example, as confirmed by the specification, SEQ ID NO:8 is not a wild-type human p40 polypeptide subunit, but a modified p40 polypeptide subunit. Comparing the level of T cell proliferation induced by SEQ ID NO:8 in the presence of a wild-type p35 polypeptide subunit of human IL-12 with the level of T cell proliferation induced by a wild-type p40 polypeptide subunit of human IL-12 in the presence of the wild-type p35 polypeptide subunit of human IL-12 cannot result in "a duplication resulting in no 4-fold increase" -- contrary to the Examiner's contentions at page 6, lines 8-9.

Similar arguments apply to claim 208. Claim 208, which depends from claim 184, specifies an isolated or recombinant polypeptide which comprises a sequence that is at least 95% identical to the full length of the mature polypeptide region of SEQ ID NO:8 and which induces a 4-fold increase in the proliferation of T cells in the presence of a mature polypeptide region of the p35 polypeptide subunit of human IL-12 compared to the proliferation of T cells induced by a mature polypeptide region of the p40 polypeptide subunit of human IL-12 in the presence of the mature polypeptide region of the human p35 polypeptide subunit. Here, too, the claimed polypeptide is not a mature polypeptide region of a wild-type human p40 polypeptide subunit, as suggested by the Examiner. For example, as indicated in the specification, a mature

polypeptide region of SEQ ID NO:8 is not the mature polypeptide region of the wild-type human p40 polypeptide subunit. Comparing the level of T cell proliferation induced by a mature region of SEQ ID NO:8 in the presence of a mature region of the wild-type human p35 polypeptide subunit with the level of T cell proliferation induced by a mature region of a wild-type human p40 polypeptide subunit in the presence of the mature region of the wild-type human p35 polypeptide subunit cannot result in "a duplication resulting in no 4-fold increase" – contrary to the Examiner's contentions at page 6, lines 8-9. To eliminate any potential confusion, claim 184 and claim 204 dependent thereon and claim 188 and claim 211 dependent thereon have been amended to specify a wild-type p35 polypeptide subunit of human interleukin-12.

Second, the Examiner's findings that "a comparison of (A) C2-22 (SEQ ID NO:1)/R2-42 (SEQ ID NO:16, modified p35 subunit) heterodimer as well as (B) C2-22 (SEQ ID NO:1/R2-157 (SEQ ID NO:24, modified p35 subunit) heterodimer both show ~ 8-fold increase compared to wild types p40 and p35 subunit heterodimers, such that a comparison of (A) and (B) would not produce a 4-fold increase" bears no relevance to the rejected claims, as they do not refer to a modified p35 subunit, but rather a wild-type p35 polypeptide subunit of human IL-12.

The Examiner concedes that there is sufficient written description support for polypeptides of the invention that induce about four-fold times greater T-cell proliferation activities in the presence of a wild-type p35 polypeptide subunit than the wild-type p40/wild-type p35 heterodimer, but contends that "there are no experimental examples that specifically state an exact 4-fold increase as recited in the claims." *Id.* at page 6. The Examiner appears to be of the view that the specification does not enable one of ordinary skill to use the invention commensurate with the scope of the claims because "further experimentation would be required to determine which heterodimer combinations resulted in exact 4-fold increases over other heterodimers." *Id.* This contention lacks merit, as the specification and data provided therein show, for example, that a C2-22/wild-type p35 heterodimer (where C2-22 corresponds to SEQ ID NO:8) exhibited about a four-fold higher proliferative activity over that of a wild-type p40/wild-type p35 heterodimer. See, e.g., page 33, line 21 to page 34, line 19; and page 139, line 26 to page 140, line 13. "About a four-fold higher proliferative activity" does not exclude "a four-fold proliferative activity."

Applicants respectfully submit that the Office Action has not met its *prima facie* burden of setting forth a reasonable explanation as to why the claims are not adequately enabled by the specification. There is clearly sufficient disclosure in the specification through illustrative examples, terminology, and discussion to teach those of ordinary skill in the art how to make and use the claimed polypeptides without an undue amount of experimentation. Moreover, that some experimentation may be necessary does not preclude enablement. The specification provides unambiguous guidance as to how to make and use the claimed polypeptides, including how to determine whether such polypeptides possess the specified activities, such as determining whether a polypeptide induces a greater increase (including a four-fold increase) in T cell proliferation activity in the presence of a wild-type human p35 polypeptide subunit compared to that induced by a wild-type human p40 polypeptide subunit and wild-type human p35 polypeptide subunit. Additionally, given the relatively high level of skill of those in the pertinent art and the state of the art at the time, one of skill would plainly have been able to make and practice the claimed invention based upon Applicants' detailed disclosure without excessive experimentation. Based upon the detailed teachings of Applicants' specification, any experimentation would certainly not be undue. Applicants respectfully submit that the Office Action has not provided a sufficient basis as to why undue experimentation would be required to practice the claimed invention.

For at least these reasons, the rejection is improper and should be withdrawn. While not conceding to the validity or correctness of this rejection, the rejection has nevertheless been mooted, because claims 208, 209, and 213-216 have been canceled without prejudice to subsequent renewal.

IV. REJECTIONS UNDER 35 USC § 112, SECOND PARAGRAPH.

Claims 204, 208, 209, and 211-216 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. *Id.* at page 7. No reasons appear to be given for the rejection of this particular set of claims. Applicants thus assume that the rejection is based upon the following findings by the Examiner.

On page 7, the Examiner states that:

> Claims 184 and 188 (lines 3 of each), 208 (line 2), and 209 (lines 1-2) recite the phrase "the polypeptide" which lacks clear antecedent basis. It is unclear if the phrase is referring to the "isolated or recombinant polypeptide" in line 1 of claims 184 or 188 [sic] or to the p35 polypeptide in lines 3 and 2, respectively, of claims 184 and 188. It is noted that the current language of the claims may be interpreted as identification of SEQ ID NO:8 as the p35 polypeptide, while SEQ ID NO:8 is stated in the specification as being a modified p40 polypeptide."

Id.

Based on these findings, the Examiner appears to reject claims 184, 188, 208, and 209. In addition, the Examiner rejects claims 185-187, 189-190, 201, 204, 207, and 210-216, due to their dependency from claims 184, 188, 208, and 209.

This rejection is respectfully traversed in part and overcome in part. The phrase "the polypeptide" in claims 184, 188, 208, and 209 clearly refers to the "isolated or recombinant polypeptide" in line 1 of each claim. The phrase "the polypeptide" cannot be confused with the phrase "p35 polypeptide," because none of these claims recites simply a "p35 polypeptide". Rather, each of these claims recites a "p35 polypeptide **subunit**" (emphasis added). Thus, antecedent basis is clear.

Nevertheless, in the interest of advancing prosecution, Applicants have amended claims 184, 186-190, 201, and 210 to substitute the "the recombinant polypeptide" for "the polypeptide" so as to alleviate any possible confusion in antecedent basis. Although the Examiner does not object to the term "isolated," this term has been deleted from the claims for conciseness. Withdrawal of the rejection of claim 184, and claims 185-187, 201, 204, and 207 dependent thereon, and claim 188, and claims 189-190 and 210-212 dependent thereon, is respectfully requested. The rejection of claims 208 and 209 has been mooted by cancellation of these claims without prejudice to subsequent renewal.

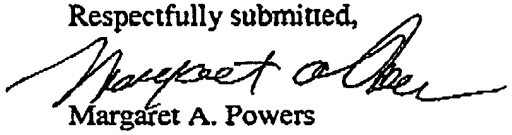
Claims 208 and 209 were rejected as they "appear to be reciting a method step involving properties of the product." *Id.* The Examiner finds that "[i]t is unclear what limitation is intended by the recitation of the intended use to further limit the product. It is unclear if the claim is a method step or if it is attempting to merely recite an inherent property of the product."

Id. Claims 213-216 were also rejected due to their dependency from claim 208 or 209. *Id.* at page 8. This rejection is respectfully traversed in part and overcome in part. Neither claim 208 nor claim 209 recites a method or an intended use. Both claims plainly specify isolated or recombinant polypeptides of the invention. The rejection has nonetheless been mooted by cancellation of these claims. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application in any way, the Examiner is invited to telephone the undersigned at (650) 298-5809.

Respectfully submitted,



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